VIA FIRST CLASS M[illegible]

I hereby certify that this paper is being depo[illegible] with the U.S. Postal Service as First Class Mail in an envelope addressed to the U.S. Patent and Trademark Office, Washington, D.C. 20231 on

July 13, 2001

FULBRIGHT & JAWORSKI L.L.P.

[signature]

PATENT & TRADEMARK OFFICE JUL 17 2001 OIPE JC34

LUD 5330.3 DIV (09901357)

RECEIVED

JUL 23 2001

TECH CENTER 1600/2900

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s)	: Rainer Zimmerman et al.
Serial No.	: 09/265,606
Filed	: March 10, 1999
For	: ISOLATED DIMERIC FIBROBLAST ACTIVATION PROTEIN ALPHA, AND USES THEREOF
Group Art Unit	: 1631
Examiner	: M. Moran

July 13, 2001

Hon. Commissioner of Patents
and Trademarks
Washington D.C. 20231

RESPONSE TO
OFFICE ACTION
(37 CFR § 1.116)

This is submitted in response to the office action dated March 26, 2001.

A one month extension of time is required, and a request with fee accompanying this response. In the office action, the examiner finally rejected all of claims 5 and 16-19, referring applicants to the arguments advanced previously, but set forth no new arguments.

Applicants have considered all of the examiner's arguments, and traverse. It is believed that the examiner has not considered this application or the pending claims completely.

Claim 5 of the application requires:

"(i) the FAPα catalytic domain...."

Now, according to the examiner, in the advisory action:

> "Although applicant has asserted in the response filed 7/10/00 that the catalytic domain consists of specific amino acid residues, such a teaching is not found anywhere in the originally filed specification or claims."

Actually, this is incorrect. See page 13, table 2 of the specification. Also, please see page 4 of the amendment of July 6, 2000, lines 19-20. Also, see the specific withdrawal of a rejection based upon alleged indefiniteness of the term "FAPα catalytic domain" and the examiner's explicit statement accepting the definition, in the office action of August 25, 2000.

Clearly, there is a definition of the domain, and it is over 100 amino acids long. Further the domain contains the structure required for catalytic activity. Ogata, et al. show that "Gly-Trp-Ser-Tyr-Gly" is required for enzymatic activity in serine hydrolases. This is also required in the catalytic domain of FAPα. One can, and must assume similar function when structures are similar. The sequences are identical in all DPPIV molecules, and in FAPα. As such, identical function must be assumed.

The examiner argues that "evidence from a similar protein (DPPIV) indicates that the catalytic domain would be internal in the structure of full length, normally folded FAPα." Actually, the "evidence" consists of an unsupported statement in the final rejection, i.e.:

> "(T)he catalytic domain, per se is commonly not available on the surface of a protein, and therefore not likely to be immunogenic."

First of all, the "evidence" referred to by the examiner has not been provided. Second, the "evidence" refers to general statements. Third, there is no evidence related to what is claimed, i.e., molecules which include a sequence of over 100 amino acids.

Essentially, what the examiner is arguing is that (i) the claimed molecules would not have enzymatic activity even though the defined, and recognized enzymatically active sequence GWSYGG is present, (ii) that the enzymatic domain would fold internally into the molecule, even though there is no evidence of this, and (iii) that even though the examiner states that it is unpredictable how the claimed molecule would fold, it is predictable that the molecule would fold such that the enzymatic domain is internal to the molecule — just as it does in the functioning, wild type molecule.

The examiner's argument attempts to have "the best of all worlds" without any evidence to support the positions taken. For example, the examiner asserts that the claimed molecule cannot be used as an

immunogen to make FAPα specific antibodies, because the FAPα region would be expected to fold internally, the way it does in naturally occurring molecules. If this assumption is true, then one has to assume that, since the molecule folds the way a naturally occurring molecule does, it will behave the way a naturally occurring molecule behaves -- and have enzymatic activity. The examiner does not wish to be bound by this position, however, and then states that the molecule would not be able to fold properly, and thus the molecule would not have enzymatic activity.

If the molecule were to fold such that the enzymatic domain were not folded internally, then it would fold such that it is external — and be available as an immunogen. The art recognizes antibodies which bind to, and inhibit enzymes, by binding, e.g., to their active sites. See, e.g., U.S. Patent No. 5,071,744 to Naujoks, et al., teaching inhibiting antibodies against alpha amylase. Clearly, the art does know how to generate antibodies against enzymatic sites, even if the enzymatic site is internally folded. The examiner's assumptions are simply not supported by evidence.

In view of the foregoing, withdrawal of the rejection, and allowance of claims 5 and 16-19 is believed proper and is urged.

Respectfully submitted,

FULBRIGHT & JAWORSKI L.L.P.

By: _____

Norman D. Hanson
Reg. No. 30,946

666 Fifth Avenue
New York, New York 10103
(212) 318-3000